510(K) SAFETY & EFFECTIVENESS SUMMARY

Submitter	EUROIMMUN US INC. 1100 The American Road Morris Plains, NJ 07950 JUL 17 2013 Tel: 973.656.1000/1.800.913.2022 Fax: 973.656.1098 Michael Locke Director of Regulatory Affairs E-mail: M.Locke@euroimmun.us
Date Prepared	July 3, 2013
Submission Type	510(k)
Device Trade/Proprietary Names	25-OH Vitamin D ELISA
Device Common/Usual Name or Classification Name	Vitamin D Test System
Classification Number/Class	21 CFR § 862.1825 - Vitamin D Test System - Class II
Product Code	MRG - Vitamin D Test system
Panel	Clinical Chemistry and Toxicology

As required by 21 CFR § 807.92, the following is in sufficient detail to provide an understanding of the basis for a determination of substantial equivalence.

510(k) Number K123660

Standard/Guidance Document Referenced (if applicable): None referenced.

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Traceability /Value Assignment of Calibrators and Controls

Traceability: As there is no international standard, the calibrators and controls are calibrated gravimetrically using UV-Vis (264nm) verified stock standards and compared with NIST standards (National Institute of Standards and Technology, USA), DEQAS (Vitamin D External Quality Assessment Scheme, UK) quality assessment data and in-house quality control sera.

Calibrators and controls are traceable to concentrations determined by UV spectrophotometric analysis. An in-house stock solution is prepared gravimetrically; and the antigen concentration is spectrophotometrically calculated using the OD coefficient of 18.2 at 264 nm to calculate the concentration from the absorbance value. This is used to build an intermediate stock volumetrically by dilution into horse serum. The intermediate stock is used in the manufacturing of lot specific calibrators and controls volumetrically.

- The calibrator levels for each batch are confirmed by running a min. of 8 quality control sera covering the whole concentration range of the calibration curve measured in a minimum of 4 runs performed by 2 different technicians on 2 different days in duplicates. The quality control sera must fall within established target ranges. Initial values for the quality control sera are assigned using the predicate device in conjunction with liquid chromatography. Once confirmation of the calibrator values is established, the new calibrators are retested by a different person for final release.
- 25-OH Vitamin D controls prepared in human serum were tested with 7 different released EUROIMMUN 25-OH Vitamin D lots, obtained from 20 independent runs, performed by 4 different persons on 9 different days. The obtained mean values were assigned as control target values. The control target ranges were assigned as mean ±3 SD (ng/mL). Target values were confirmed using two predicate devices (k021163; k112725) and a HPLC method.

Calibrators and controls are supplied in liquid form and are horse serum based with active ingredients of 0.09% ProClin 950 and 0.09% sodium azide. Avoid skin contact. Calibrators are 25-OH vitamin D3 spiked. No special treatment necessary for the use of the calibrators and controls except reagents must be mixed thoroughly before use either manually or by vortexing.

Caution: The serum contained in the calibrators and controls are of animal origin (horse). Handle kit reagents as if capable of transmitting an infectious agent. Appropriate precautions and good laboratory practices must be used in the storage, handling and disposal of the kit reagents. Disposal of kit reagents should be in accordance with local regulations.

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Value Assignments: Target ranges for control materials are: C1 (low): 15 ng/mL (10-25 ng/mL) and C2 (high): 40 ng/mL (25-60 ng/mL). Testing and assignment of values involves a min. of 5 assays from a min. of 2 operators with 8 replicates, resulting in a min. of 40 determinations. The mean obtained values are assigned as control values. The controls are labeled with the assigned values as mean C1 ±50% and C2 ±30%.

Calibrator value assignments are based on an internal procedure; the initial value assignment for calibrators was performed using 2 predicate assays (k021163; k112725) and HPLC. The final values are verified & assigned by adjusting their initial values to meet the specified ranges when tested against the predicate assays. Once confirmation of the values is established, the new calibrators are tested again in bulk and final.

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Device Description

EUROIMMUN 25-OH Vitamin D ELISA consists of a microwell ELISA plate coated with (sheep) monoclonal anti-25-OH vitamin D antibodies, 6 calibrators, 2 controls, Biotin, sample buffer, enzyme conjugate, wash buffer concentrate, TMB chromogen/substrate solution and stop solution.

This ELISA test kit is designed for the in vitro determination of 25-OH vitamin D in human serum or plasma samples. In the first analysis step, the calibrators and patient samples are diluted with biotin-labelled 25-OH vitamin D and added to microplate wells coated with (sheep) monoclonal anti-25-OH vitamin D antibodies. During the incubation an unknown amount of 25-OH vitamin D in the patient sample and a known amount of biotin-labelled 25-OH vitamin D compete for the antibody binding sites in the microplate wells plate. Unbound 25-OH vitamin D is removed by washing. For the detection of bound biotin-labelled 25-OH vitamin D, a second incubation is performed using peroxidase-labelled streptavidin. In a third incubation using the peroxidase substrate tetramethylbenzidine (TMB) the bound peroxidase promotes a colour reaction. The colour intensity is inversely proportional to the 25-OH vitamin D concentration in the sample. Results for the samples can be calculated directly using a standard curve.

Antibodies: sheep monoclonal antibodies which identify specifically 25-OH vitamin D3 and 25-OH vitamin D2.

Intended Use/ Indications for Use

EUROIMMUN 25-OH Vitamin D ELISA is intended for the quantitative determination of 25-OH Vitamin D and other hydroxylated vitamin D metabolites in human serum and plasma (EDTA, Li-heparin). Results are to be used in conjunction with other clinical and laboratory data to assist the clinician in the assessment of vitamin D sufficiency in adult populations.

Indication(s) for Use:
Same as intended use.

Special Conditions for the Use Statement(s):
For prescription use only.

Special Instrument Requirements:
Microwell plate reader capable of measuring OD at 450nm and at 620nm for dual wavelength readings.

Substantial Equivalence:

Predicate Device Name(s):
IDS Immunodiagnostic Systems Ltd. OCTEIA 25-Hydroxy Vitamin D

Predicate 510(k) Number(s):
K021163

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510(K) SAFETY & EFFECTIVENESS SUMMARY, Continued

Comparison of Assays, Similarities and Differences

The following table compares the EUROIMMUN 25-OH Vitamin D ELISA Test System with the Equivalence - predicate device.

Similarities

Item	New Device	Predicate Device
Intended Use/ Indication for Use	For the quantitative determination of 25-OH Vitamin D and other hydroxylated vitamin D metabolites in human serum or plasma. Results are to be used in conjunction with other clinical and laboratory data to assist the clinician in the assessment of vitamin D sufficiency in adult populations.	Same
Sample Type	Serum and Plasma	Same
Test Format	96-well microplate assay	Same
Assay Components	Microtiterplate; Calibrators; Biotin labeled 25-OH Vitamin D; Avidin-Conjugate; Assay buffer; Washbuffer; Substrate; Stop solution	Same
Instrument	ELISA plate reader	Same
Measuring Wavelength	450/620nm	Same
Approximate Assay Time	3.5 hours	Same
Antigen Used in Calibrators	25-OH Vitamin D3	Same
Assay Principle	Competitive immunoassay	Same
Reagent Storage Temperature	2-8 °C	Same
Test Methodology	Samples are diluted with buffer containing a reagent dissociating Vitamin D metabolites from its binding protein. The diluted samples are incubated in microtiter wells which are coated with sheep anti-25-OH vitamin D antibodies for 2 hours at room temperature before aspiration and washing. Peroxidase labeled avidin is added and binds to the captured biotin, following a further wash step, color is developed using a chromogenic substrate (TMB). Color intensity is inversely proportional to the concentration of 25-OH vitamin D.	Same
Interpretation of Results	Standard curve	Same
Traceability	Standardized using UV quantification of 25-OH vitamin	Same
Specificity	25-OH Vitamin D and other hydroxylated vitamin D metabolites	Same

Differences

Item	New Device	Predicate Device
Antibody	Monoclonal sheep anti-25-OH-Vitamin D IgG antibody	Polyclonal sheep anti-25-OH-Vitamin D IgG antibody
Calibrators	6	7
Assay range	4.0 – 120 ng/ml	2.4 – 144 ng/ml
Sample Volume	20 µl	25 µl

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Performance Characteristics

Precision/Reproducibility:

The reproducibility of the test was investigated following CLSI standard EP05-A2. Intra- and Inter-Assay coefficients of variation (CV) were determined using samples with values at different points on the calibration curve. All samples were natural serum samples collected freshly in-house from obvious healthy blood donors. After initial screening, 2 of 8 samples (No. 7 and 8) were spiked. All samples were then aliquoted and stored at -20°C. The intra-Assay CVs are based on 40 determinations and the Inter-Assay CVs on 40 determinations performed in 10 different runs on 5 different days (with 4 replicates per run) according to the package insert. Acceptance criterion was that the CV's show results below 12% for samples over 10 ng/ml and results below 20% for concentrations below 10 ng/ml. The following results were obtained:

Intra-Assay Reproducibility

Sample No.	1	2	3	4	5	6	7	8
Mean (ng/mL):	4.1	16.8	24.6	28.8	42.9	46.3	68.7	93.3
SD.	0.5	0.9	1.7	2.1	1.8	2.8	3.5	6.3
CV,%	12.4	5.5	6.9	7.4	4.2	6.0	5.1	6.7

Inter-Assay Reproducibility

Sample No.	1	2	3	4	5	6	7	8
Mean (ng/mL):	5.8	16.6	22.3	34.8	43.5	55.3	67.8	94.4
SD.	0.9	1.3	1.8	3.1	3.0	3.7	5.8	7.8
CV,%	16.2	7.8	8.1	8.8	7.0	6.7	8.6	8.3

The lot-to-lot reproducibility of the test was investigated following CLSI standard EP05-A2. Inter-lot coefficients of variation (CV) were determined using samples with values at different points on the calibration curve. All samples were natural serum samples collected freshly in-house from obvious healthy blood donors. After initial screening, 2 of 8 samples (No. 7 and 8) were spiked. The inter-lot CVs are based on 32 determinations performed in 8 different runs on 4 different lots (with 2 runs per lot and 4 replicates per run) according to the package insert. Acceptance criterion was that the CV's show results below 12% for samples over 10 ng/ml and results below 20% for concentrations below 10 ng/ml. The following results were obtained:

Lot to Lot Reproducibility

Sample No.	1	2	3	4	5	6	7	8
Mean (x):	7.3	18.5	24.8	37.4	47.6	58.0	74.3	97.3
SD.	0.89	1.89	1.81	2.29	4.25	4.07	6.59	9.26
CV,%	12.2	10.2	7.3	6.1	8.9	7.0	8.9	9.5

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510(K) SAFETY & EFFECTIVENESS SUMMARY, Continued

Limit of Blank, Limit of Detection and Functional Sensitivity: Limit of blank (LoB), limit of detection (LoD) and functional sensitivity (FS) were investigated following CLSI standard EP17-A.

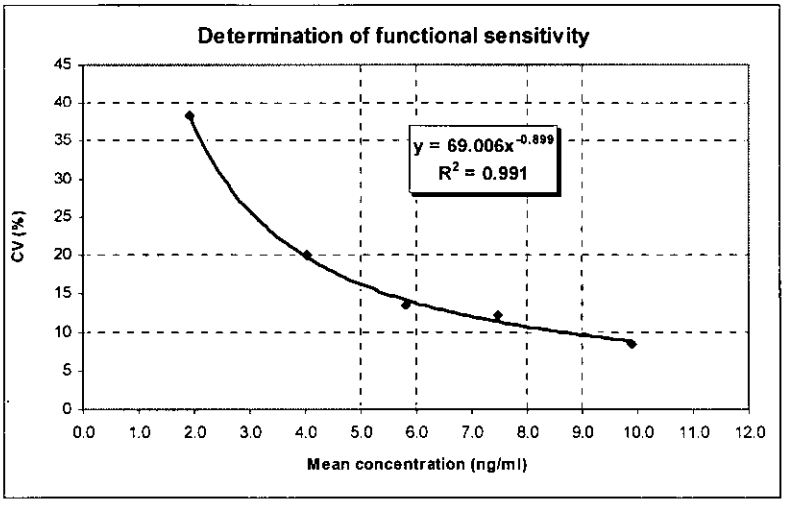
LoB was determined as the concentration corresponding to the mean OD of the zero calibrator minus 1.645 times the standard deviation using the mean of 60 replicates for calibrator 1 (0 ng/ml) and the mean of 20 replicates for calibrator 2 (4 ng/ml). LoB was found to be 0.4 ng/ml.

μ_B (OD)	2.721
σ_B (OD)	0.038
μ_{C1} (OD)	2.721
μ_{C2} (OD)	2.146
LoB (OD)	2.658
LoB (ng/ml)	0.43

LoD was determined as the LoB plus 1.645 times the standard deviation of 200 determinations from 5 samples in the low range of 2 to 10 ng/ml, measured in 5 independent runs with 8 replicates per run. The mean LoD was found to be 1.8 ng/ml.

Sample	1	2	3	4	5
Concentration (ng/ml)	2.0	4.0	6.0	8.0	10.0
σ_S (ng/ml)	0.731	0.810	0.783	0.919	0.834
LoD (ng/ml)	1.63	1.76	1.72	1.94	1.80
Mean LoD (ng/ml)	1.8				

Functional sensitivity is defined as the lowest concentration at which the potential regression line crosses the 20% CV line and was determined from a plot of the mean concentrations (X-axis) vs. % CVs (Y-axis). Functional sensitivity was found to be 4.0 ng/ml. Results below 4 ng/mL are reported as "< 4 ng/mL".



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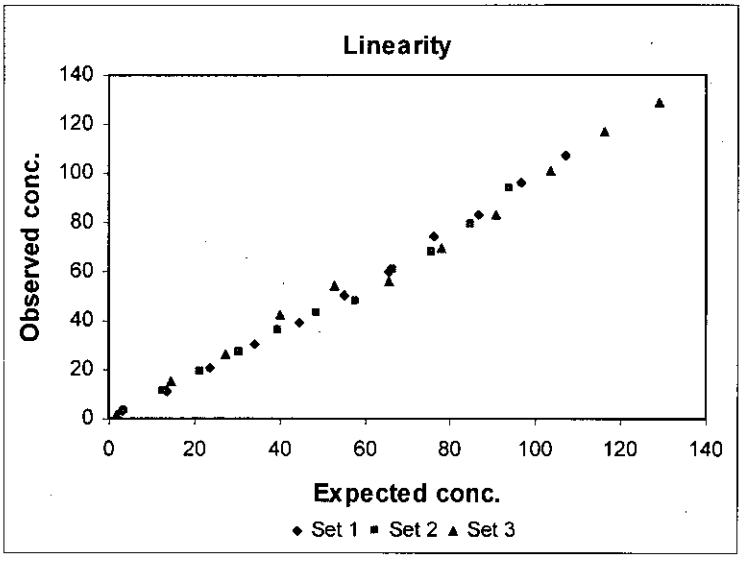
Linearity/Assay Reportable Range:
The linearity of the test was investigated following CLSI standard EP6-A. Sets of 11 sample preparations were prepared by mixing a natural negative sample (0 ng/ml) and high positive samples. The sample preparations covered the concentration range of 2 to 129 ng/ml. Each set was run according to the package insert in the same run in double determinations per sample preparation, the mean of the two determinations for each sample was calculated and polynomial regression was performed of observed results vs expected results. Although visually the data demonstrated a linear relationship, the p-values of the polynomial regression coefficients were significant (< 0.05) for two of the three sample sets. However, the amount of non-linearity above the functional sensitivity of 4.0 ng/ml was found acceptable below 15%. The detailed results are shown below. Based on the results of the linearity study and limit of detection study, it can be concluded that the assay is sufficiently linear from 4.0 to 120 ng/ml.



Regression $y=ax^3+bx^2+cx+d$		Set 1				Set 2				Set 3			
		Coeff.	Std. error of slope	p-value	Std. error of regr.	Coeff.	Std. error of slope	p-value	Std. error of regr.	Coeff.	Std. error of slope	p-value	Std. error of regr.
linear	c	1.01	-	-	2.12	0.96	-	-	3.02	0.98	-	-	4.38
	d	-3.25	-	-		-2.09	-	-		-0.57	-	-	
	R^2	0.997	-	-		0.990	-	-		0.999	-	-	
2nd order poly-nomial	b	0.00	0.00	0.00	1.03	0.00	0.00	0.01	2.05	0.00	0.00	0.13	3.98
	c	0.81	-	-		0.67	-	-		0.79	-	-	
	d	0.24	-	-		2.46	-	-		3.23	-	-	
	R^2	0.999	-			0.996	-	-		0.993	-	-	
3rd order poly-nomial	a	0.00	0.00	0.10	1.03	0.00	0.00	0.06	1.43	0.00	0.00	0.20	3.56
	b	0.00	0.00	0.36		-0.01	0.00	0.02		-0.01	0.00	0.12	
	c	0.73	-	-		1.10	-	-		1.17	-	-	
	d	0.93	-	-		-0.95	-	-		-0.31	-	-	
	R^2	0.999	-	-		0.998	-	-		0.995	-	-	

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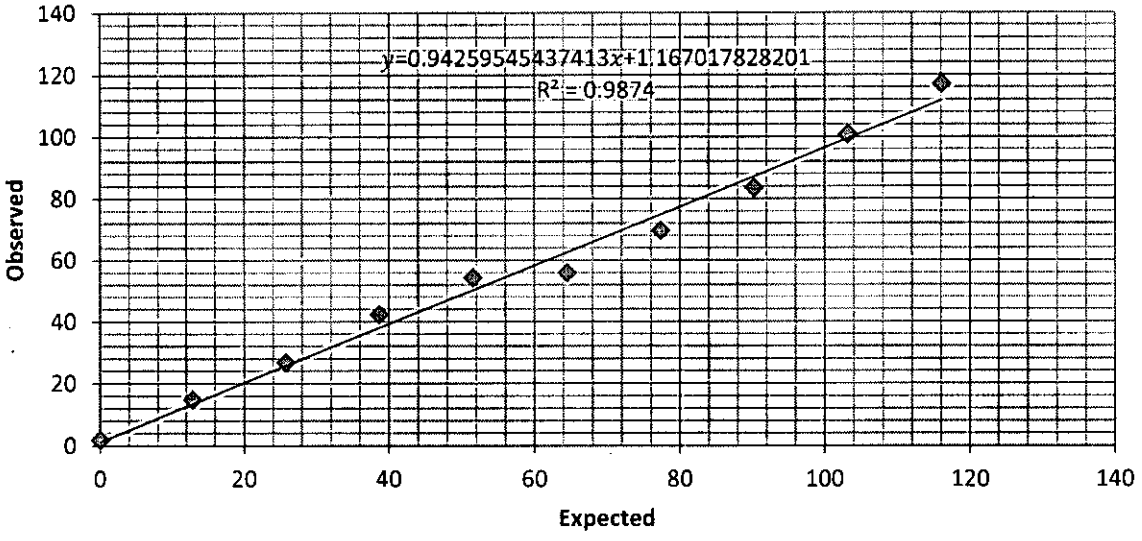
Linearity Graph w/Representative Data (Set 3)



Regression Data

x	y	$x \times y$	x^2
$\sum_{i=1}^{n} x_i$=584.80	$\sum_{i=1}^{n} y_i$=562.90	$n\sum_{i=1}^{n} x_i y_i$=45822.52	$\sum_{i=1}^{n} x_i^2$=47889.10

Regression Calculations

slope m,

$$m = \frac{n\sum_{i=1}^{n} x_i y_i - \sum_{i=1}^{n} x_i \sum_{i=1}^{n} y_i}{\sqrt{\left(n\sum_{i=1}^{n} x_i^2 - (\sum_{i=1}^{n} x_i)^2\right)}} = 0.94259545437413$$

intercept b,

$$b = \frac{\sum_{i=1}^{n} y_i - m\sum_{i=1}^{n} x_i}{n} = 1.167017828201$$

$$y = mx + b$$

$$y = 0.94259545437413x + 1.167017828201$$

Standard Deviation

The deviation of the measurement $\square_{\square}$ from the mean is $\square_{\square} = \square_{\square} - \overline{\square}$

Uncertainties in the Slope & Intercept

Standard error in the slope σ_m:

$$\sigma_m^2 = \frac{n\sigma_y^2}{n\sum_{i=1}^{n} x_i^2 - (\sum_{i=1}^{n} x_i)^2} = 0.0019 \; ; \; \sigma_m = \pm 0.0438$$

Standard error in the intercept σ_b:

$$\sigma_b^2 = \frac{\sigma_y^2 \sum_{i=1}^{n} x_i^2}{n\sum_{i=1}^{n} x_i^2 - (\sum_{i=1}^{n} x_i)^2} = 9.1833 \; ; \; \sigma_b = \pm 3.0304$$

Standard deviation of y_i:

$$\sigma_i^2 = \sigma_y^2 = \frac{\sum_{i=1}^{n}(y_i - b - mx_i)^2}{n-2} = 26.2521; \; \sigma_y = \pm 5.1237$$

Correlation Coefficient: $r = \frac{n\sum_{i=1}^{n} x_i y_i - \sum_{i=1}^{n} x_i \sum_{i=1}^{n} y_i}{\sqrt{\left(n\sum_{i=1}^{n} x_i^2 - (\sum_{i=1}^{n} x_i)^2\right)\left(n\sum_{i=1}^{n} y_i^2 - (\sum_{i=1}^{n} y_i)^2\right)}} = 0.99147705552933$

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Analytical Specificity

Cross-Reactivity:

Cross reactivity was investigated following Abraham et al (Handbook of radioimmunoassay, 1977). A 25-OH Vitamin D free sample was aliquoted and spiked with potential cross reacting Vitamin D metabolites at the concentrations listed below. The following cross reactivities were observed. The study shows that the 25-OH Vitamin D ELISA detects both 25-OH Vitamin D3 and 25-OH Vitamin D2 as well as other hydroxylated Vitamin D metabolites as stated in the intended use. Expected concentrations of 1,25-OH Vitamin D3 and 1,25-OH Vitamin D2 in natural samples are below 100 pg/ml, so the obtained cross reactivity has no significant influence on results of 25-OH Vitamin D.

Potential Cross-Reacting Substance	Molecular Weight (g/mol)	Conc. Spiked (ng/ml)	Conc. Observed (ng/ml)	Cross Reactivity (%)
25-OH Vitamin D3	400.64	10.0	10.0	100
25-OH Vitamin D2	412.65	25.0	24.3	100
24,25-OH Vitamin D3	416.64	100	0.3	0.3
Cholecalciferol (Vit. D3)	384.64	10,000	3.4	0.03
Ergocalciferol (Vitamin D2)	396.65	10,000	5.1	0.05
1,25-OH Vitamin D3	416.64	10.0	4.3	45
1,25-OH Vitamin D2	428.65	10.0	19.8	212
3-epi-25-OH Vitamin D3	400.64	10.0	1.7	17

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Interference:
Interferences were investigated following CLSI standard EP07-A2. To investigate the influence from hemoglobin, triglycerides and bilirubin as well as from cholesterol, biotin and ascorbic acid, sera at different 25-OH Vitamin D concentrations were spiked with potential interfering substances and incubated with the test system according to the package insert. The recovery in relation to the unspiked sample without interferent was calculated. The individual recovery was within the accepted individual recovery of 90 – 110 %. No significant interference was observed for concentrations of up to 750 mg/dl for hemoglobin, 2000 mg/dl for triglycerides, 40 mg/dl for bilirubin and up to 400 mg/dl for cholesterol, 1000 mg/dl for biotin and 10.0 mg/ml for ascorbic acid.

Significant interference (above 10 % deviation from unspiked sample) was seen with 1000 mg/dl of hemoglobin.

Potential interfering substance	Range of sample concentration	Range of recoveries (%)
Hemoglobin (0, 250, 500 and 750 mg/dl)	15.0 – 71.6 ng/ml	90 – 110 %
Triglycerides (0, 500, 1000 and 2000 mg/dl)	16.2 – 51.0 ng/ml	98 – 110 %
Bilirubin (0, 10, 20 and 40 mg/dl)	13.0 – 54.9 ng/ml	90 – 109 %
Cholesterol (0, 200 and 400 mg/dl)	9.6 – 27.3 ng/ml	94 – 109 %
Biotin (0, 10, 100 and 1000 mg/dl)	21.0 – 74.7 ng/ml	91 – 107 %
Ascorbic acid (0, 2.5, 5.0, 7.5 and 10.0 mg/ml)	13.0 – 56.1 ng/ml	94 – 110 %

Assay Cut-off:
Not Applicable

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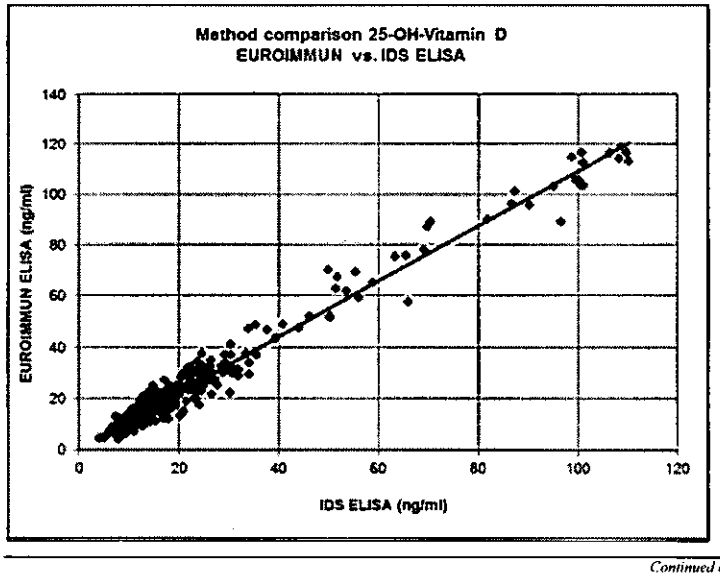
Comparison Studies

Method Comparison w/Predicate Device:
The method comparison against the predicate device was performed following CLSI standard EP09-A2. Both the predicate device and the subject device were performed exactly as described by their respective instructions for use.

Serum samples were obtained from different sources (141 prospective samples sent in for 25-OH-Vitamin D testing from a clinical laboratory, 28 samples from 25-OH-Vitamin D quality assessment programs (harvested from blood donated by patients undergoing therapeutic venesection for hemochromatosis or polycythemia), 5 samples from a 25-OH-Vitamin D quality control panel (untreated routine patient material) and 30 samples from normal blood donors). All patients have given their informed consent. These samples are native (natural) and not treated or adjusted in any way.

To ensure that the tested concentrations of 25-OH Vitamin D are distributed across the reportable measurement range, 36 samples (15%) in the set were spiked with 25-OH Vitamin D stock solution of 25-OH Vitamin D3. In total, 240 samples were collected, ranging from 4.1 to 119.1 ng/ml, and tested with the EUROIMMUN 25-OH Vitamin D ELISA and with a FDA-cleared reference assay. Results of linear regression analysis are shown in the table below.

n	240
Concentration Range (Predicate)	4.1 – 110.4 ng/ml
Concentration Range (Candidate)	4.1 – 119.1 ng/ml
Regression Equation (y = Candidate, x = Predicate) 95% C.I. of Intercept 95% C.I. of Slope	y = 0.78 + 1.08 x -0.06 – 1.63 1.06 – 1.11
Correlation Coefficient R 95% C.I. of R	0.9858 0.9817 – 0.9890



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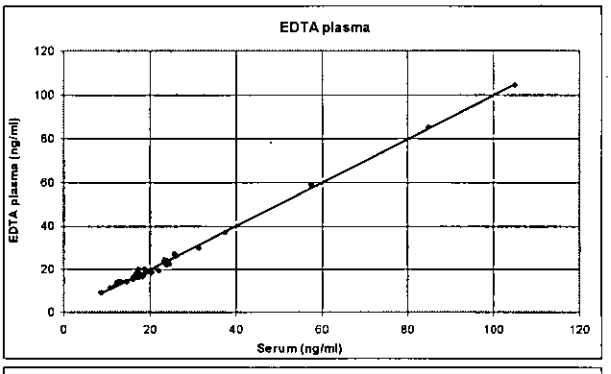
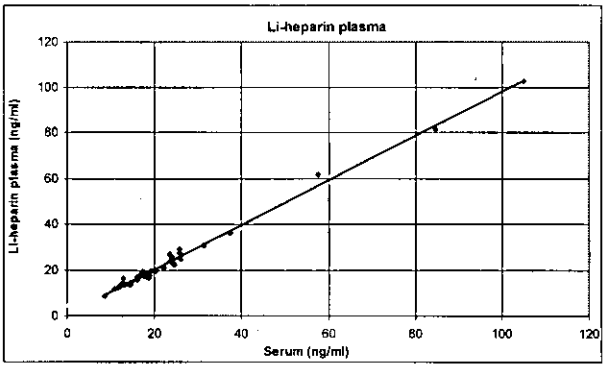
Matrix Comparison

The usability of plasma was investigated using sample pairs each of serum and corresponding plasma (EDTA, Li-heparin) from donors. To ensure that the tested concentrations of 25-OH Vitamin D are distributed across the reportable dynamic range, 3 sample pairs in the set were spiked with 25-OH Vitamin D stock solution of 25-OH Vitamin D3. Passing-Bablok regression was calculated for the comparison of serum to plasma. The regression equation is near the ideal correlation (intercept 0; slope 1.0) indicating equivalence of concentrations between serum and the corresponding plasma matrices. Coefficients of determination were found to be above 0.99 and %recovery compared to serum was in the range of 87 to 127 % (serum = 100 %).

	EDTA plasma	Li-heparin plasma
n	38	38
Concentration Range (Serum)	8.6 – 105.1 ng/ml	8.6 – 105.1 ng/ml
Concentration Range (Plasma)	8.8 – 104.2 ng/ml	8.5 – 102.6 ng/ml
Regression Equation: (y = plasma, x = serum) 95% C.I. of intercept 95% C.I. of slope	y = 0.29 + 0.99 x -0.37 – 1.18 0.93 – 1.02	y = 0.55 + 0.97 x -0.65 – 1.33 0.93 – 1.04
Coefficient of determination R^2	0.996	0.993
Mean %recovery Range of %recovery	100 % 87 – 116 %	101 % 87 – 127 %





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510(K) SAFETY & EFFECTIVENESS SUMMARY, Continued

Expected Values/Reference Range

Reference intervals were established following CLSI standard C28-A3. The levels of 25-OH vitamin D were analyzed in a panel of 206 samples from healthy subjects (70 men and 136 women with an average age of 64 years; age range: 22 – 99 years) from a US commercial source. The samples are known to be from normal US blood donors from the US Midwest region and were drawn in early October 2010. The observed median, minimum and maximum values as well as the 2.5% and 97.5% percentiles were similar to those reported for other devices cleared in the US (e.g. K102432, K112725, K110619, K091849, K110586, K071480). The results are shown in the table below.

	(ng/ml)	(nmol/l)
Minimum	< 4	< 10
Maximum	64.8	162.0
Mean	20.8	51.9
Median	19.4	48.4
2.5% Percentile	5.4	13.6
97.5% Percentile	47.0	117.4

This data is provided for guidance only. It is important for each laboratory to establish its own reference ranges, representative of its typical population. Also published studies representing the local population can be taken into consideration.

Interpretation criteria are provided by the US CDC/NCHS National Health and Nutrition Examination Surveys (NHANES):

Status	(ng/ml)	(nmol/l)
At risk of vitamin D deficiency	< 12	< 30
At risk of vitamin D inadequacy	12 – 19	30 – 49
Sufficient in vitamin D	20 – 50	50 – 125
Possibly harmful vitamin D	> 50	> 125

[1]Looker AC, Johnson CL, Lacher DA, Pfeiffer CM, Schleicher RL, Sempos CT. Vitamin D status: United States, 2001–2006. NCHS data brief, no 59. Hyattsville, MD: National Center for Health Statistics. 2011.

The Endocrine Society Clinical Practice Guideline (2011) recently suggested a higher target level of at least 30 ng/ml:

Status	(ng/ml)	(nmol/l)
Deficiency	< 20	< 50
Insufficiency	20 – 29	50 – 75
Sufficiency	30 – 100	75 – 250

[2]Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metabol 96 (2011) 1911-1930.

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510(K) SAFETY & EFFECTIVENESS SUMMARY, Continued

Stability Studies

Stability studies are conducted following the international standard EN 13640:2002: Stability testing of in vitro diagnostic reagents.

Real-time testing at 2-8°C and accelerated testing at 37°C were conducted for all kit components (Biotin, Conjugate, Microtiterplate, control materials and the calibrators). The stability study protocol and the acceptance criteria are shown below. The predicted shelf-life, based on results of accelerated testing at 37°C, is at least 12 months at 2-8°C for the control materials and the calibrators. Real-time stability testing is on-going to support the predicted shelf-life of 12 months at 2-8°C.

The stability study protocol and the acceptance criteria to determine open-vial stability of the complete kit are shown below. Open-vial stability of the kit is 3 months when stored at 2-8°C. Biotin was found to be stable for at least 2 weeks when diluted to working strength.

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510(K) SAFETY & EFFECTIVENESS SUMMARY, Continued

Conclusion

The data presented is complete and provides a reasonable assurance to support the basis of the claim for substantial equivalence. The labeling is sufficient and satisfies the requirements of 21 CFR § 809.10.

The EUROIMMUN 25-OH Vitamin D ELISA assay (including calibrators and controls) is substantially equivalent to other products presently in commercial distribution intended for similar use; and has been demonstrated to be safe and effective. Most notably, the EUROIMMUN 25-OH Vitamin D ELISA is substantially equivalent to the currently marketed IDS Immunodiagnostic Systems Ltd. OCTEIA 25-Hydroxy Vitamin D (K021163) for in vitro diagnostic use for the quantitative determination of 25-OH Vitamin D and other hydroxylated vitamin D metabolites in human serum and plasma (EDTA, Li-heparin). The EUROIMMUN 25-OH Vitamin D ELISA assay is to be used in conjunction with other clinical and laboratory data in the assessment of vitamin D sufficiency in adult populations.

Michael Locke	Michael Locke/Director of Regulatory Affairs	7/3/2013
Signature	*Printed Name/Title*	*Date*

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

July 17, 2013

EUROIMMUN US INC.
C/O Michael Locke
1100 The American Road
MORRIS PLAINS NJ 07950

Re: K123660
Trade/Device Name: 25-OH Vitamin D ELISA
Regulation Number: 21 CFR 862.1825
Regulation Name: Vitamin D test system
Regulatory Class: II
Product Code: MRG
Dated: June 06, 2013
Received: June 07, 2013

Dear Mr. Locke:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for

the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Carol C. Benson -S for

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): k123660

Device Name: 25-OH Vitamin D ELISA

Indications for Use:

EUROIMMUN's 25-OH Vitamin D ELISA is intended for the quantitative determination of 25-OH Vitamin D and other hydroxylated vitamin D metabolites in human serum and plasma (EDTA, Li-heparin). Results are to be used in conjunction with other clinical and laboratory data to assist the clinician in the assessment of vitamin D sufficiency in adult populations.

Prescription Use __X____ And/Or Over the Counter Use ____.
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostics and Radiological Health (OIR)

Yung W. Chan -S

Division Sign-Off
Office of In Vitro Diagnostics and Radiological Health

510(k)___k123660_____